Remarks

The Office Action mailed April 8, 2003 has been received and reviewed. Claims 39-43 having been amended, the pending claims are claims 35 and 38-43.

Claims 39-43 have been rewritten in independent form.

Reconsideration and withdrawal of the rejections are respectfully requested.

Rejection under 35 U.S.C. §102

The Examiner rejected claim 38 under 35 U.S.C. §102(e) as allegedly being unpatentable over U.S. Pat. Application Publication No. 2003/0054436 (Kunsch et al.). Applicants respectfully traverse the rejection.

"[F]or anticipation under 35 U.S.C. 102, the reference must teach *every aspect* of the claimed invention either explicitly or impliedly." M.P.E.P. §706.02 (emphasis added).

Kunsch et al. disclose genes and polypeptides derived from *Staphylococcus aureus*. However, Kunsch et al. fail to explicitly or impliedly teach *every aspect* of the presently claimed invention. For example, the disclosure of Kunsch et al. fails to enable one of skill in the art to make or use "[a] crystal of *Staphylococcus aureus* nicotinamide adenine dinucleotide (*S. aureus* NAD) synthetase" (e.g., claim 38).

The Examiner alleged that "the proteins can be isolated by freeze-thaw cycling of microbial cells used for recombinant production. This would result in a crystal of the protein." Applicants respectfully traverse the Examiner's allegation.

Applicants respectfully submit that it would be obvious to one of skill in the art that freeze-thaw cycling of microbial cells does not necessarily result in a crystal of a polypeptide. "Protein crystallization is mainly a trial-and-error procedure in which the protein is *slowly* precipitated from its solution" (Jan Drenth, *Principles of Protein X-Ray Crystallography*, page 1 (1994), emphasis added). Thus, rapid freezing of a polypeptide solution might result, for example, in the formation of an oily or amorphous material, but not necessarily a crystal.

Further, the United States Patent and Trademark Office stated, in commenting on the patentability of a hypothetical claim ("A crystalline form of protein P having unit cell dimensions of a=4.0nm, b= 7.8nm, and c= 11.0nm," Case 4, Trilateral Project WM4 on *Comparative study on "protein 3-dimensional (3-D) structure related claims"*), the following:

> ***With respect to novelty, it is recognized in the art that a crystal of protein P is different from previously known forms of protein P.*** Furthermore, the claim complies with the nonobviousness requirement of 35 U.S.C. § 103 because as noted in the fact pattern, there was no prior art reference teaching or suggesting a crystal of protein P or related proteins. (emphasis added).

Trilateral Project WM4 on *Comparative study on "protein 3-dimensional (3-D) structure related claims*," Annex 3, Case 4, A4 (http://www.uspto.gov/web/tws/wm4/pdf/wm4_3d_annex_3.pdf). Thus, Applicants respectfully submit that Kunsch et al. fail to teach or suggest a crystal of *S. aureus* NAD synthetase, or a method of making the crystal. Thus, claim 38 is neither anticipated by, nor obvious over, Kunsch et al.

In light of the remarks presented herein above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §102.

Rejection under 35 U.S.C. §103

The Examiner rejected claims 35 and 38 under 35 U.S.C. §103(a) as allegedly being unpatentable over *Crystal Screen* (Hampton Research) taken in view of U.S. Pat. Application Publication No. 2003/0054436 (Kunsch et al.). Applicants respectfully traverse the rejection.

"To establish a prima facie case of obviousness . . . there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. . . . The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's

disclosure." M.P.E.P. §706.02(j). "To establish a *prima facie* case of obviousness . . . the prior art reference (or references when combined) must teach or suggest all the claim limitations." M.P.E.P. §706.02(j). Applicants respectfully submit that the documents cited by the Examiner, alone or in combination, fail to teach or suggest all the claim limitations.

Kunsch et al. disclose "polynucleotide sequences of the genome of *Staphylococcus aureus*, polypeptide sequences encoded by the polynucleotide sequences, corresponding polynucleotides and polypeptides, vectors and hosts comprising the polynucleotides, and assays and other uses thereof" (Abstract). However, Kunsch et al. fail to suggest or disclose, among other things, methods of purifying *S. aureus* NAD synthetase, methods of crystallizing *S. aureus* NAD synthetase, and crystals of *S. aureus* NAD synthetase.

Likewise, *Crystal Screen* (Hampton Research) lacks a disclosure of methods of purifying *S. aureus* NAD synthetase, methods of crystallizing *S. aureus* NAD synthetase, and crystals of *S. aureus* NAD synthetase.

Therefore, Kunsch et al. in view of *Crystal Screen* (Hampton Research) fail to teach or suggest all the claim limitations (e.g., a method for crystallizing *S. aureus* NAD synthetase and a crystal of *S. aureus* NAD synthetase), and Applicants respectfully submit that the Examiner has failed to present a *prima facie* case of obviousness.

Furthermore, neither Kunsch et al. nor *Crystal Screen* (Hampton Research) include a teaching or suggestion to make a crystal of *S. aureus* NAD synthetase. Applicants respectfully submit that the Examiner is improperly basing the rejection on an "obvious to try" standard. *See, for example,* M.P.E.P. §2143.01: "The mere fact that references can be combined does not render the resultant combination obvious unless the prior art also suggest the desirability of the combination." (section entitled "FACT THAT REFERENCES CAN BE COMBINED OR MODIFIED IS NOT SUFFICIENT TO ESTABLISH *PRIMA FACIE* OBVIOUSNESS").

Specifically, "Crystal Screen™ is a complete reagent kit designed to provide a rapid screening method for the crystallization of biological macromolecules. Crystal Screen is a

straightforward, effective, and practical kit for determining *preliminary crystallization conditions*." (First paragraph of Crystal Screen™ user guide, Hampton Research, 2000-2002; emphasis added). However, the Crystal Screen reagent kit provides no teaching or suggestion as to the selection, from the myriad of biological molecules, of a specific biological macromolecule that might be amenable to crystallization using the reagent kit. Specifically, Crystal Screen reagent kit provides no teaching or suggestion that *S. aureus* NAD synthetase can be crystallized using the reagent kit. The Crystal Screen reagent kit, a tool for use in the hands of one of skill in the art, may be capable of providing guidance to one of skill in the art in the determination of *preliminary crystallization conditions* for a biological macromolecule which has also been selected by one of skill in the art. However, the Crystal Screen reagent kit alone does not purport to be capable of determining useful, final crystallization conditions. Thus, the Crystal Screen reagent kit fails to provide motivation for one of skill in the art to provide crystals or methods of crystallizing *S. aureus* NAD synthetase.

Finally, in commenting on the patentability of a hypothetical claim ("A crystalline form of protein P having unit cell dimensions of a=4.0nm, b= 7.8nm, and c= 11.0nm," Case 4, Trilateral Project WM4 on *Comparative study on "protein 3-dimensional (3-D) structure related claims*"), the United States Patent and Trademark Office stated the following:

> ***Although there is a general desire to obtain the crystal structure of any protein, the methodology of doing so is highly unpredictable and specific to each individual protein. Therefore, without guidance in the art as to how to crystallize a particular known protein, the known protein in crystalline form would be nonobvious***. (emphasis added).

Trilateral Project WM4 on *Comparative study on "protein 3-dimensional (3-D) structure related claims*," Annex 3, Case 4, A4 (http://www.uspto.gov/web/tws/wm4/pdf/wm4_3d_annex_3.pdf).

Based on the remarks presented herein above, Applicants respectfully submit that the Examiner has failed to stablish a *prima facie* case of obviousness. Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §103.

Allowable Subject Matter

Applicants note that claims 39-43 were listed as being rejected in the Office Action Summary mailed April 8, 2003. However, no reasons for rejections of claims 39-43 were included in the body of the Office Action mailed April 8, 2003.

Claims 39-43 have been rewritten in independent form. Applicants respectfully request notification of the allowability of claims 39-43 in the next Official Communication.

Summary

It is respectfully submitted that all the pending claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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July 8, 2003
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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that this paper is being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Assistant Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 8th day of JULY, 2003, at 4:33 pm (Central Time).

By: _____
Name: SAM HEBE

APPENDIX A - SPECIFICATION/CLAIM AMENDMENTS INCLUDING NOTATIONS TO INDICATE CHANGES MADE
Serial No.: 09/772,598
Confirmation No. 2967
Docket No.: 6315.N

Amendments to the following are indicated by underlining what has been added and bracketing what has been deleted. Additionally, all amendments have been indicated by the use of bold typeface.

In the Claims

For convenience, all pending claims are shown below.

35. A method for crystallizing *Staphylococcus aureus* nicotinamide adenine dinucleotide (*S. aureus* NAD) synthetase comprising:

providing purified *S. aureus* NAD synthetase at a concentration of about 1 mg/ml to about 50 mg/ml; and

crystallizing *S. aureus* NAD synthetase from a solution comprising about 5% by weight to about 50% by weight polyethylene glycol (PEG) and about 0% by weight to about 20% by weight dimethyl sulfoxide (DMSO).

38. A crystal of *Staphylococcus aureus* nicotinamide adenine dinucleotide (*S. aureus* NAD) synthetase.

39. **(Amended)** **A[The]** crystal of ***Staphylococcus aureus* nicotinamide adenine dinucleotide (*S. aureus* NAD) synthetase[claim 38]** having the trigonal space group symmetry $P2_1$.

40. **(Amended)** **A[The]** crystal of ***Staphylococcus aureus* nicotinamide adenine dinucleotide (*S. aureus* NAD) synthetase[claim 38]** comprising a unit cell having dimensions of a, b, and c; wherein a is about 40Å to about 60Å, b is about 90Å to about 120Å, and c is about 80Å to about 110Å; and wherein $\alpha = \gamma = 90°$ and β is about 80° to about 120°.

41. **(Amended)** **A[The]** crystal of ***Staphylococcus aureus*** **nicotinamide adenine dinucleotide (*S. aureus* NAD) synthetase[claim 38]** comprising atoms arranged in a spatial relationship represented by the structure coordinates listed in Table 1.

42. **(Amended)** **A[The]** crystal of ***Staphylococcus aureus*** **nicotinamide adenine dinucleotide (*S. aureus* NAD) synthetase[claim 38]** having amino acid sequence SEQ ID NO:1.

43. **(Amended)** **A[The]** crystal of ***Staphylococcus aureus*** **nicotinamide adenine dinucleotide (*S. aureus* NAD) synthetase[claim 38]** having amino acid sequence SEQ ID NO:1, with the proviso that at least one methionine is replaced with selenomethionine.